

**REMARKS/ARGUMENTS****I. Introduction**

Claims 36-48 and 51-86 are pending and stand rejected. Applicants herewith cancel claims 66, 68, 76, and 86. With the entry of this amendment, claims 36-48, 51-65, 67, 69-75, 77-85 will be pending and active.

**II. The Examiner's Rejections****A. Rejection of claim 76 under 35 USC § 112, second paragraph**

The Examiner rejects claim 76 for the asserted reason that the recitation of "said lower compartment" lacks proper antecedent basis in claim 64. Applicants assert that this rejection is moot in view of the cancellation of claim 76.

**B. Rejection of claims 36-48, 51-63 and 71-86 under 35 USC § 112, first paragraph**

The Examiner rejects claims 36-48, 51-63 and 71-86, asserting that while the specification enables a centrifugation vessel comprising a porous barrier, filter sieve or the flap as described in Figure 3, the specification does not provide enablement for a centrifuge vessel comprising any other type of "flap." Examiner Canella further states that "[t]he instant method and product claims are dependent in part or in whole on a centrifugation vessel having a flap by which to divide the vessel into an upper and lower compartment. The specification teaches that the flap is closed in the state when the vessel is at rest and opened by centrifugal force during centrifugation...."(Office Action at page 2, last paragraph)

In response to this rejection, applicants have amended claims 36 and 71 to add that the flap comprises an outer edge and the flap opens into the lower compartment from the outer edge and is closed in the state when the centrifugation is at rest and open during centrifugation. This is in accordance with the Examiner's discussion of the claimed flap, as noted above, and is

supported by the specification at page 12, lines 22-25. In view of this amendment, Applicants respectfully request the Examiner to withdraw this rejection.

**C. Rejection of claims 64-67 under 35 USC § 102(b)**

The Examiner rejects claims 64-67 as being anticipated by Suda *et al*, U.S. Patent No. 4,391,802. Applicants respectfully traverse this rejection.

Suda *et al* disclose mouse myelogeneous leukemia cells (MI) which were cultured, treated, harvested and separated using Ficoll-Urografin density gradients. In contrast, the invention of claims 64-67 is directed to a kit for the separation of tumor cells from a body fluid. Cultured cells are not the same as cells from a body fluid, such as blood or ascitic fluid etc. (Specification at page 7, lines 19-30.) Additionally, Suda *et al*. teaches the use of a density gradient of Ficoll-urografin having three different densities (col. 3, lines 4-7). The present invention uses a separation media that has one density within a specific range, as recited in claim 64.

In view of these distinctions, applicants respectfully request the examiner to reconsider and withdraw the rejection over Suda *et al*.

**D. Rejection of claims 64 and 65 under 35 USC § 102(e)**

The Examiner has rejected claims 64 and 65 as being anticipated by Jones *et al*, U.S. Patent No. 6,051,393. According to the Examiner, Jones discloses a cell separation medium and centrifugation vessel, wherein said cell separation medium has a density of 1.055 (column 8, lines 57-60).

Applicants respectfully traverse this rejection. However, in further response, applicants have amended claim 64 to recite a density in the range of 1.059 to 1.061 g/ml. As such, Jones

does not teach each and every element of the claimed invention and the Examiner's rejection should be withdrawn.

**E. Rejection of claims 64, 65 and 68 under 35 USC § 102(b)**

The Examiner has rejected claims 64, 65 and 68 under 35 USC § 102(b) over Asgari *et al.*, U.S. Patent No. 5,629,147. According to the Examiner, Asgari *et al.* teaches a cell separation medium and a centrifugation vessel, wherein said cell separation medium has a density of 1.065 (Column 31, Table 10.)

Applicants respectfully traverse this rejection. However, in further response, applicants point out that the amended claims recite a density range of 1.059 to 1.061 g/ml. Because Asgari *et al.* teaches a density that falls outside this range, this reference does not teach each and every claimed element. Accordingly, applicants respectfully request the Examiner to withdraw this rejection.

**F. Rejection of claims 64 - 68 and 70 and 76 under 35 USC § 102(b)**

The Examiner has rejected claims 64 - 68 and 70 and 76 under 35 USC § 102(b) over Van Vlasselaer *et al.*, U.S. Patent No. 5,474,687. According to the Examiner, Van Vlasselaer discloses a Percoll cell separation medium having a density of 1.0605, plus or minus 0.00005 g/ml in the bottom of a cell-trap tube with body fluid in the upper portion of the tube (column 13, lines 32-52).

Applicants respectfully traverse this rejection. Van Vlasselaer discloses a method for enriching CD34<sup>+</sup> cells from apheresed blood, but does not disclose the separation of tumor cells from a body fluid, as set forth in claim 64 and incorporated into the dependent claims. Accordingly, this reference does not teach each element of the claimed invention and the

rejection for lack of novelty should be withdrawn. The rejection of claims 68 and 76 is moot in view of the cancellation of these claims.

**G. Rejection of claims 64, 65, 68 and 69 under 35 USC § 102(e)**

The Examiner has rejected claims 64, 65, 68 and 69 under 35 USC § 102(e) over Mond *et al.*, U.S. Patent No. 5,932,427. According to the Examiner, Mond *et al.* disclose a cell separation medium and a centrifugation vessel, wherein the cell separation medium has a density of 1.062 (Column 14, lines 13-17).

Applicants respectfully traverse this rejection. However, in further response, applicants point out that claim 64 now recites a density range of 1.059 to 1.061. Because the density taught in Mond *et al.* is outside this range, Mond *et al.* fails to teach each and every element of claim 64 or the dependent claims. Accordingly, applicants respectfully request that this rejection be withdrawn.

**H. Rejections Under the Judicially Created Doctrine of Obviousness-Type  
Double Patenting**

The Examiner has rejected claims 36-38 and 51-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27, 28, 29 30, 31, 48 and 49 of U.S. Patent No. 6,821,726 ("the '726 patent") in view of Van Vlasselaer, U.S. Patent No. 5,474,687.

The Examiner explains that the instant claims are an obvious variant over the claims in the '726 patent because Van Vlasselaer teaches that having a barrier between the cell separation medium and blood is an improvement over prior art methods because it increases the recovery of separated cells because the desired cells can be decanted rather than removed by a pipette. The

Examiner concludes that Van Vlasselaer would have motivated the skilled artisan to use the instant methods in order to obtain a higher yield of the separated tumor cells.

Applicants respectfully traverse this rejection and argue that one of skill in the art would not have been motivated to combine Van Vlasselaer with the '726 patent to arrive at the present invention. This is so because Van Vlasselaer teaches a product that is quite different from what applicants claim. That is, Van Vlasselaer teaches a centrifugation tube which has an upper and lower compartment, which are separated by an annular member disposed in the tube, wherein the member has an area less than the area of the cross-section of the tube (see claim 26). The barrier, filter, sieve or flap according to the present invention, in contrast to the centrifugation vessel of Van Vlasselaer, does not display a hole in the member which separates the compartments. At the time before and after the centrifugation, the centrifugation vessel of the present invention separates the separation medium from the body liquid, whereas the layers in the centrifugation tube of Van Vlasselaer are always connected through the hole in the annular member. Due to undesired shaking of the centrifugation vessel described by Van Vlasselaer, before or after centrifugation, the separated layers might be mixed with each other. As applicants have previously asserted, when read as a whole, the claims in the '726 patent do not suggest the methods of the present application. And, nothing in Van Vlasselaer cures this deficiency. Accordingly, applicants respectfully request the Examiner to withdraw this obviousness type double patenting rejection.

### **III. Conclusion**

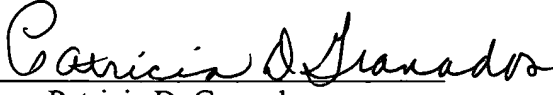
In view of the above amendments and remarks, it is respectfully submitted that the remaining claims are in condition for allowance. Early notice of allowance is earnestly solicited.

The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

Date: August 17, 2006

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